--matrix anchor protein--.

**REMARKS**

Claim 57 has been amended to correct an inadvertent error of transcription. Claims 57-60 remain before the Examiner. Applicants respectfully request reconsideration and reexamination of those claims in light of the comments to follow.

Rejections Under the Second Paragraph of 35 U.S.C. § 112

The Examiner has rejected claims 57 under the second paragraph of 35 U.S.C. § 112 as allegedly being indefinite. In view of the amendment to the claim 57, this rejection should no longer apply.

Obviousness-Type Double Patenting

The Examiner has rejected claims 57-60 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims of U.S. Patent No. 5,627,024. Enclosed herewith is a Terminal Disclaimer wherein the Applicants disclaim patent protection extending beyond the period of protection afforded to U.S. Patent No. 5,627,024.

Rejections Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 57-60 under the first Paragraph of 35 U.S.C. § 112 for an alleged lack of enablement. Applicants respectfully argue against this rejection for the reasons of record as well as the reasons set forth below.

The present invention provides a vector for use in expressing, on the surface of a phage, a preselected polypeptide. Surface expression is accomplished by expressing the preselected polypeptide in the form of a fusion protein linked to an anchor

matrix protein of the phage.

Prior to the time of the present disclosure, skilled artisans were unable to produce libraries of polypeptide expression useful for high throughput screening. The present disclosure is the first to describe means of surface expressing of such preselected polypeptides wherein the expressed polypeptides retains its biological function. Because the biological function of the expressed polypeptide is maintained, and the polypeptide exists on the surface of a phage, the expressed polypeptide can be subjected to high throughput screening without the need for any additional steps or procedures. In addition, because of the ability of the skilled artisan to reproduce high numbers of phages, the present disclosure provides an ability to produce high numbers of expressed polypeptides.

The recited elements of the presently pending claims provide those conditions necessary and sufficient for carrying out the invention. Basically, a skilled artisan need only to produce an expression vector in accordance with the claimed instructions. As is the case with all vectors and is well known to those of skill in the art, the vector contains promoters and ribosome binding sites to enable transcription and translation, and a termination or suppressor codon to direct expression of the encoded polypeptide or, in this case, a fusion protein. The elements of the expressed fusion protein are an anchor matrix protein, the desired polypeptide, and a peptide linker linking the anchor matrix protein and the desired polypeptide. Nucleotide sequences encoding the anchor matrix protein, desired polypeptide and linker are aligned properly. The claimed elements describe such proper alignment.

In his rejection, the Examiner points out that for any particular anchor matrix protein and desired polypeptide, the specification does not teach whether fusion occurs at the N- or C-

terminus of those components. As is known to a skilled artisan in the field, the proper alignment and expression of the desired polypeptide depends upon the locus of biological function. By way of example, if the biological function of the desired polypeptide resides at or near the N-terminus of that polypeptide, fusion preferably takes place through the C-terminus of that polypeptide. Making such a determination is well within the ordinary skill of one in the art. Similarly, it may be necessary to alter the length of the linker between the anchor matrix protein and the desired polypeptide to maximize availability of the biological function of the expressed polypeptide on the surface of the phage. Applicants respectfully submit that selection of a given length of a linker is well within the skilled artisan's repertoire.

As evidence that the present disclosure is enabling for anchor matrix proteins other than pV, applicants have submitted a paper by Mikawa, et al. showing use of the disclosed methods and compositions for expressing a desired polypeptide fused to the anchor matrix protein, pD. With regard to that publication, the Examiner points out certain differences between the teachings of that disclosure and the Examples of the present application. In particular, the Examiner points out that, in the publication, fusions were made between the second and third codons rather than after the initial codon as exemplified in the present application. Applicants point out that the precise location of the fusion is not a critical element of the claimed invention. All that matters, is that the initial start codon (e.g., Met) occurs before the insertion point. As long as the initiation codon is maintained, insertion can take place after the second, third, fourth, etc. codon. The precise selection of the insertion point is routine. The Examiner points out that one of the authors of the publication, namely Mikawa is not a named inventor of the instant application. If anything, Applicants respectfully submit

that this shows that persons of ordinary skill in the art (not the inventors) can take the teaching of the instant application and accomplish the stated goals.

Finally, Applicants point out that the use of conditional suppression or conditional fusion as set forth in the present disclosure and claims minimizes concerns about phage disruption, which alleged concerns appear to be a strong basis for the Examiner's rejection. Using conditional fusion, both fused and unfused polypeptides are expressed. In this way, in a single study, it is easy for a skilled artisan to determine whether phage disruption occurred to a significant extent. In summary, Applicants submit any experimentation that may be required to practice the present invention is routine in nature and certainly within the repertoire of the skills of an artisan in the field.

**SUMMARY**

In view of the amendments to the claims and for the reasons set forth above, Applicants respectfully submit that the claims are now in a condition of allowance. An early notification to that effect is hereby earnestly solicited.

Respectfully submitted,

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DATE

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